Recommednations for Medications (continued)

β-Blocker (Annotation K)	Dose Range	Comments/Cautions
Cardioselective Metoprolol	Initial 6.25 mg (see comments) qd/bid; titrate slowly to 12.5-25 mg bid to target 50-75mg bid	• Cardioselectivity is dose related • Caution should be used when using β-adrenergic blockers in patients with systolic dysfunction • Low initial doses should be implemented • Use slow gradual increases in the dosage • Effects are generally seen in 3-12 months • Low dosages of metoprolol immediate-release are not commercially available, although various methods of titration have been used;[i] low dose metoprolol XL is available for titration; consult with pharmacy for options • Do not use in patients with bronchospastic disease, symptomatic bradycardia, or advanced heart block without a pacemaker • Should not be abruptly discontinued • Carvedilol should be given with food to reduce the incidence of orthostatic hypotension; consider separating the ACEI, adjusting dose of diuretic, or temporary ACEI dose reduction if dizziness occurs
Metoprolol XL	Initial 12.5-25mg qd; double dose every 2 wks to target dose 200mg qd (or as tolerated)	
Bisoprolol	Initial 1.25mg qd; increase by 1.25mg q wk until 5mg qd, then increase by 2.5mg q 4 wks to target 10mg qd	
α & β antagonist Carvedilol[h]	Initial 3.125 mg bid, range 6.25-25 mg bid (patients ≥ 85 kg may be titrated to 50mg bid); titrate at minimum of q 2 wks to target 25-50mg mg bid	

Drug	Dose Range	Comments/Cautions
Digoxin (Annotation L)	Initial = 0.125 mg qd Range = 0.0625-0.375 mg qd	Trough serum digoxin levels should be monitored if: • HF worsens or renal function deteriorates • Signs of toxicity develop (e.g., confusion, nausea, vomiting, abdominal pain, diarrhea, anorexia, fatigue, arrhythmias, visual disturbances) • Dose adjustments are made • Medications added that affect digoxin concentration (e.g., quinidine, verapamil, amiodarone, antibiotics, anticholinergics)
Spironolactone (Annotation M)	Initial = 25mg qd Range = 25mg qod-50mg qd	• Potential side effects include gastrointestinal, gynecomastia, hyperkalemia, menstrual irregularities • Hyperkalemia occurs more frequently in patients on K+ supplements and patients with renal insufficiency • K+ supplements should be avoided with spironolactone unless hypokalemia develops • Use with caution in patients with renal insufficiency • Schedule follow-up electrolytes (check K+ q 4 wks for first 3 months, then q 3 months for first yr and then q 6 months) and renal function after initiation and dose adjustments • Use with caution in patients receiving ACEIs due to the potential for hyperkalemia

Bold = National Formulary item

Adapted from Hebel SK, ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons Inc., 1999; Heart failure: Management of patients with left ventricular systolic dysfunction. Clinical Practice Guideline, No. 11. Rockville, MD. U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research. AHCPR Publication No. 94-0613; McEvoy GK, ed. American Hospital Formulary Service Drug Information, Bethesda, MD:American Society of Health-System Pharmacists, Inc., 1999.

[a] Higher doses have been effective and tolerated

[b] Unless patients have persistent hypokalemia or are being treated with low dose spironolactone for severe HF (Annotation M), potassium-sparing diuretics should not be used in combination with ACEI (Appendix 1)

[c] The brand names of metolazone are not bioequivalent, therefore doses vary

[d] Intermittent use recommended once the response of the patient is stabilized

[e] Target doses for HF were derived from major trials and AHCPR guidelines. Excluding captopril and enalapril, doses for HF reflect doses used to increase exercise tolerance in HF patients

[f] One hour before meals, on an empty stomach

[g] Cohn JN, Johnson G, Ziesche S et al. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. N Engl J Med 1991;325:303-10.

[h] Carvedilol is FDA approved for the treatment of mild-moderate HF stabilized on standard therapy

[i] Eichhorn EJ, Bristow MR. Practical guidelines for initiation of beta-adrenergic blockade in patients with chronic heart failure. Am J Cardiol 1997;79:794-8

The Pharmacologic Management of Chronic Heart Failure

Pharmacy Benefits Management-Strategic Healthcare Group and Medical Advisory Panel (PBM-MAP

Pocket Guide

Patient with suspected HF[a,b]

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Assess medical history and physical exam; diagnose and evaluate patient. A diagnosis of HF due to systolic dysfunction (defined as LVEF of ≤ 40%) can be made by 2-dimensional echocardiogram with Doppler flow studies; other tests (e.g., radionuclide ventriculography) may be used to determine left ventricular systolic function, non-invasively *(Annotations A, B)*

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Implement nonpharmacologic interventions; manage concomitant cardiac condition/address underlying cause *(Annotation C)*

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Consider anticoagulation with warfarin in patients with A Fib[b] or history of thromboembolism *(Annotation D)*

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For patients with diastolic dysfunction, manage according to recommendations *(Annotation E)*

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IF	THEN
Systolic dysfunction with symptoms of volume overload	Add a diuretic; titrate to euvolemic state *(Annotation G)*
Diagnosis of systolic dysfunction	Add ACEI[b], titrate to target dose *(Annotation H)*
ACEI intolerant	Consider HYD[b]/ISDN[b] or AIIRA[b] *(Annotations I, J)*
NYHA[b] class I HF	Continue present management; schedule regular follow-up *(Annotation N)*
NYHA class II-III HF	Add a ß-blocker; titrate to target dose *(Annotation K)*
Level of functional status not acceptable	Add digoxin (if no bradycardia) *(Annotation L)*
Level of functional status not acceptable and recent NYHA class IV HF and current class III or IV symptoms	Consider spironolactone *(Annotation M)*
Acceptable level of functional status (For patients with continued symptoms, refer to a cardiologist or consider the additional of other controversial therapies)	Continue present management; schedule regular follow-up *(Annotation N)*

[a] Cardiology referral may be requested at any point in treatment

[b] HF=heart failure; A Fib=atrial fibrillation; ACEI=angiotensin-converting enzyme inhibitor; HYD=hydralazine; ISDN=isosorbide dinitrate; AIIRA=angiotensin II receptor antagonist; NYHA=New York Heart Association

VA access to full guideline: http://www.oqp.med.va.gov/cpg ***August 2001***

DoD access to full guideline: http://www.cs.amedd.army.mil/Qmo

Written & illustrated by the Pharmacy Benefits Management-Medical Advisory Panel (PBM-MAP)

Sponsored & produced by the VA Employee Education System

Symptoms of HF	Signs of HF
Shortness of breath (SOB)	Tachycardia
Cough	Increasing weight
Orthopnea	Jugular venous distention (JVD) or hepatojugular reflux
Paroxysmal nocturnal dyspnea (PND)	Presence of S_3 (third heart sound)
Dyspnea on exertion (DOE)	Laterally displaced apical impulse
Edema	Pulmonary crackles or wheezes
Fatigue	Hepatomegaly
Weight gain	Peripheral edema

Recommended Tests to Assist in the Diagnosis of HF
Creatinine (Cr), Blood urea nitrogen (BUN), Serum electrolytes, Urinalysis, Albumin, Bilirubin, Prothrombin time, Complete blood count (CBC), Thyroid stimulating hormone (TSH) Electrocardiogram, Chest radiography

NYHA Functional Classification
Class I: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina.
Class II: Slight limitation of physical activity. Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
Class IV: Unable to carry on any physical activity without discomfort. Symptoms are present at rest. With any physical activity, symptoms increase.

Adapted from the Criteria Committee of the American Heart Association. 1994 revisions to the classification of functional capacity and objective assessment of patients with disease of the heart. Circulation 1994;90:644-5.

General Principles for Management of HF:

- Goals of therapy include improved symptoms, increased functional capacity, improved quality of life, slowed disease progression, decreased need for hospitalization, and prolonged survival.
- Educate patients and family on the etiology, prognosis, therapy, dietary restrictions, activity, adherence, and signs and symptoms of recurrent HF.
- Discuss nonpharmacologic therapy including abstaining from alcohol and tobacco, limiting dietary sodium, reducing weight if appropriate, and participating in exercise training programs.
- Increase pharmacologic therapy as tolerated in an effort to achieve target doses.
- Emphasize adherence to the medication regimen.
- Schedule regular follow-up and assess for change in functional status.
- Cardiology referral may be requested at any point in the care of the patient. Some facilities may have interdisciplinary HF disease management clinics to provide continuity of care for patients with HF.

Specific Recommendations for Medications in the Treatment of HF

ACEI (Annotation H)	Initial dose (Target doses[c])	Comments/Cautions
Captopril[f]	12.5 mg tid (50 mg tid)	• Start with lower or less frequent doses in patients with renal insufficiency
Enalapril	2.5 mg bid (10mg bid)	• CrCl < 30 mL/min, initial dose 2.5mg qd
Fosinopril	10 mg qd (20-40 mg qd)	• Start with 5mg qd if moderate to severe renal failure
Lisinopril	5 mg qd (20-40 mg qd)	• CrCl < 30 mL/min, initial dose 2.5mg qd
		Contraindications to all ACEI • History of angioedema or other documented hypersensitivity to an ACEI; bilateral renal artery stenosis or renal artery stenosis in a solitary kidney; symptomatic hypotension; pregnancy; serum potassium > 5.5 mEq/L that cannot be reduced
Drug (Annotation I)	**Dose Range**	**Comments/Cautions**
Hydralazine	initial= 75 mg/d (3-4 divided doses); range= 75-300 mg/d (3-4 divided doses); (ave. dose V-HeFT II 200 mg/d[g])	• Monitor adverse effects: dizziness, headache, lupus-like syndrome, nausea, tachycardia, postural hypotension • Advise patient to take with food
Isosorbide dinitrate	initial= 30 mg/d (3 divided doses); range=30-160mg/d (3 divided doses); (ave. dose V-HeFT II 100 mg/d[g])	• Monitor adverse effects: flushing, headache, postural hypotension, rash • May cause an increase in ocular pressure; caution with presence of glaucoma
AIIRA (Annotation J)	**Dose Range**	**Comments/Cautions**
Candesartan 4, 8, 16, 32mg tablets	8-32mg divided qd-bid	• All AIIRAs are contraindicated in 2nd and 3rd trimesters pregnancy due to potential neonatal/fetal morbidity and death • Use AIIRAs with caution in patients with renal artery stenosis • Initiate losartan at 25mg and use telmisartan with caution in patients with hepatic impairment • An AIIRA should be used with caution, if at all, in patients who have previously experienced angioedema with an ACEI
Irbesartan 75, 150, 300mg tablets	75-300mg qd	
Losartan 25, 50mg tablets	25-100mg divided qd-bid	
Telmisartan 40, 80mg tablets	40-80mg qd	
Valsartan 80, 160mg capsules	80-320mg qd	